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(21) International Application Number: PCT/SE99/00820 (22) International Filing Date: 12 May 1999 (12.05.99) (30) Priority Data: 9801700-7 14 May 1998 (14.05.98) SE (71) Applicant (for all designated States except US): INTER-HEALTH AB [SE/SE]; Kungsängsvägen 27, S-561 51 Huskvarna (SE). (72) Inventors; and (75) Inventors/Applicants (for US only): KÄRNERUD, Lars [SE/SE]; Sommarfågelsvägen 2, S-560 27 Tenhult (SE). ÖLMESKOG, Stellan [SE/SE]; Skogsgatan 8, S-578 31 Aneby (SE). (74) Agents: BERGVALL EFTRING, Stina, Lena et al.; Dr Ludwig Brann Patentbyrå AB, P.O. Box 17192, S-104 62 Stockholm (SE).		(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i>
(54) Title: USE OF SHARK LIVER OIL FOR LOCAL TREATMENT OF SKIN DISEASES OF DOMESTIC ANIMALS (57) Abstract <p>The invention relates to the use of shark liver oil comprising alkyl glycerols for the preparation of a drug for local treatment of skin diseases of domestid animals as well as method of treatment.</p>		

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USE OF SHARK LIVER OIL FOR LOCAL TREATMENT OF SKIN DISEASES OF DOMESTIC ANIMALS

The present invention relates to the use of shark liver oil comprising alkyl glycerols for the preparation of a drug for the local treatment of skin diseases of domestic animals e.g. horses, cattle, sheep, dogs and cats as well as a method of treatment of skin diseases of domestic animals. Such diseases are for example summer sore, sarcoids, such as Equine sarcoids, favus and scurf of different origin, greasy heels, mud fever, rain scalds, saddle sore, girth galls, and ringworm.

BACKGROUND OF THE INVENTION

In ancient times shark liver oil, extracted e.g. from Greenland shark and from the so called Seamouse, *Chimera monstrosa*, was used within the traditional medicine for a variety of therapeutic purposes, such as combating weakness and irritation of the respiratory and digestive organs, gland diseases, bee stings and wound healing, etc.

Crude shark liver oil contains squalene, etherlipids (alkyl glycerols) and triglycerides. The composition of the oil varies widely from one shark species to another. In some species the oil contains as much as 90% squalene, while the ether lipids or the triglycerides dominate in other.

Due to their varying properties, compounds derivable from the shark liver oil have found applications within the various fields of use.

US 50 79 003 A to Scaffidi A. discloses creams or lotions incorporating emulsions of fish oils, such as shark liver oil, squalane, and squalene that are used as moisturisers, as hand and body lotions and as sunburn preventives. Cosmetic and moisturising compositions are described also comprising numerous other ingredients.

In US 3 294 639 to Chalmers et al, the oral or parenteral use of alkylglycerols, more specifically batyl alcohol, chimyl alcohol and selachyl alcohol, in the treatment of inflammatory diseases in warm-blooded animals is disclosed.

However, there is nothing disclosed or suggested in prior art about the unexpected advantages obtained by the local application of shark liver oil on the skin of domestic animals such as horses suffering from skin diseases. Diseases which successfully are treated with the drug according to the invention are e.g. summer sore; sarcoids, such as Equine sarcoids; favus and scurf of different origin such as those emerging by infection with *Dermatophilus*, e.g. dermatophilosis; greasy heels, mud fever, rain scalds, saddle sore, girth galls; and ringworm.

Summer sore is a skin disease affecting domestic animals, mainly horses, associated with itching and involving loss of hair with running, ulcerous skin. The background to summer sore is not entirely clear but it is believed to be associated with sun shine and heat, but may also depend on allergic reactions to insect bites. It is usually treated in that the horse is covered with a horse-cloth and stabled, the latter especially by night. Treatment with cortisone preparation which alleviates the pain has also been suggested. Other alternatives are treatment with some homeopathic preparations e.g. one named Ökozon added to the fodder of the animal or an oil called "PROB oil" comprising root extracts, herbs, oils and char coal. However, there remains a need for a preparation that gives a quick healing, is cheap and effective.

Equine sarcoids are fibroblastic skin tumours and papillomas, attributed to viruses such as retro- and papillom viruses. There are several types of sarcoids with different appearance, some flat and fleshy, other forming wart-like bumps. The tumours do not spread in the body but might spread locally in the skin and cause considerable inconveniences. The lesions are notoriously difficult to treat due to infiltrative growth, with multiple lesions resulting in high rates of recurrence. One way of treatment has been by surgery or laser surgery, other freezing, immunotherapy, radiation treatment, hyperthermia, brushing with etching substances or injection with cytotoxic drugs directly into the tumour.

Dermatophilus congolensis causing dermatophilosis, penetrates into the skin when it is softened due to wet surroundings or cracked under dusty and dry conditions and makes the skin scurfy. The treatment available hitherto has been to remove the scurf, cut the hair, shampoo the affected

area with anti-septic shampoo and to apply antibiotic ointment. Sometimes also injections of antibiotics have been necessary.

Ringworm is the name of a group of fungal diseases of the skin of man and domestic animal marked by the formation of ring-shaped pigmented patches covered with vesicles and scales and caused by dermatophytes. In order to get ride of ringworm not only the animal but the whole stable as well as the equipment must be disinfected. However, eventually, the animal becomes immune to the disease but the inconveniences during the primary stage are considerable.

The problem to be solved by the present invention, thus, is to provide a preparation which in a simple and effective way by local application cure the diseases mentioned above.

DEFINITION OF THE INVENTION

The above presented problem is solved by the present invention which relates to the use of shark liver oil for the preparation of a drug for the local treatment of skin diseases of domestic animals such as e.g. horses, cattle, sheep, dogs and cats etc. The shark liver oil used for the preparation of the drug is crude or refined shark liver oil comprising alkyl glycerols in an amount of up to 100 % and used in a concentration of from 1 to 100 %. Other ingredients that may be added to the shark liver oil to enhance the penetration of the active compound into the skin, to preserve it and to make it convenient to handle, are selected from acidifying agents, emollients, emulsifying agents, surfactants, preservatives, viscosity controlling agents, anti-oxidants, solvents, etc.

The skin diseases which may be treated with the drug according to the invention are e.g. summer sore, sarcoids such as Equine sarcoids, favus and scurf of different origin such as those emerging with infections by *Dermatophilus*, e.g. dermatophilosis, greasy heels, mud fever, rain scalds, saddle sores, girth galls, and ringworm.

The preparation according to the invention alleviates the itch of summer sore and gives a clear improvement after a treatment period of 2 to 5 days and eventually, completely healed after continuous treatment during at least one week.

A suitable treatment frequency of summer sore is by local application of the preparation to the affected area 2 to 3 times per week during at least one week.

Sarcoids were treated by the local application of the preparation according to the invention on the skin of the animal once daily and when a clear improvement was noticed the preparation was applied twice a week.

Substances included in the preparation are e.g., acidifying agents, emollients, emulsifying agents, surfactants, preservatives, viscosity controlling agents, anti-oxidants, solvents, etc.

An agent suitable as emulsifier, emollient and surfactant is e.g. Tefose 2561 comprising PEG-6 stearate (50-72%), Ceteth-20 (10-24.9%), Glyceryl stearate (5-9.9%), and Steareth-20 (5-9.9%), included in amounts of up to 30 %

Useful as preservatives and acidifiers are all substances accepted of the man skilled in the art for veterinary medicine treatment. Suitable examples are sorbic acid, lactic acid, salicylic acid, or other α -hydroxy acids, each in amounts of up to 10 %.

Among suitable anti-oxidants, e. g. ascorbyl palmitate can be mentioned, however all anti-oxidants acceptable within the art of veterinary medicine and known to the man skilled may be used. The amounts included are decided according to stability test results in line with established practise.

The preparation can be in any form suitable for topical application such as an ointment, a cream, a milk, a lotion, a liquid emulsion, a spray, an aerosol or a powder.

The preparation may be applied to the skin in any suitable way such as by rubbing, spraying, the application of liquid impregnated patches, drenched plasters, etc.

All embodiments disclosed in the appending claims are herewith included in the specification.

All percentages stated are by weight unless otherwise stated.

The invention will now be described by the following non-limiting examples.

EXAMPLE 1

Preparation in the form of a cream for the treatment of summer sore.

PHASE A

Tefose 2561	12.00%
Ecomer oil	9.00%
Ascorbyl palmitate	0.05%

PHASE B

Water	73.80%
Glycerol	5.00%
Sorbic acid	0.15%
Total	100%

The water phase (B) is heated under stirring to 75°C and slowly added to the oil phase under stirring. The mixture is cooled to 20°C.

EXAMPLE 2

A further preparation was prepared according to Example 1 from

CITHOROL 2621	6.00%
Bentone gel	18.00%
Ecomer oil	32.00%
Paraffin wax	6.00%
Sorbic acid	0.15%
Water	37.85%
Total	100%

EXAMPLE 3

The preparation is a sprayable lotion prepared in accordance with Example 1.

PHASE A

Tefose 2561	3.80%
Ecomer oil	2.00%
Ascorbyl palmitate	0.05%

PHASE B

Water	89.00%
Glycerol	5.00%
Sorbic acid	0.15%
Total	100%

EXAMPLE 4

In case the animal has rubbed of all or almost all of the fur a drenched patch or plaster should be applied comprising substantially neat shark liver oil, which however has to be stabilised.

Ecomer oil	99.98%
ROXAN A	0.02%

The composition of the additives included in the preparation are as follows:

Ecomer oil is shark liver oil, the active substance and emollient.

CITHOROL 2621 is a polyglyceryl-3-di-isostearate an emulsifying agent.

Bentone gel consists of stearalkonium hectorite, a viscosity controlling agent, caprylic/capric triglyceride, an emollient, and propylene carbonate, a solvent.

ROXAN A comprises (dl- α -tocopherol 5%, ascorbyl palmitate 25% and lechitine 70%) and act as stabiliser.

TEFOSE 2561 consists of PEG-6 stearate (50-70.2%) an emulsifying agent; Ceteth-20 (10-24.9%) an emulsifying agent and surfactant; Glyceryl stearate (5-9.9%) an emulsifying agent and Steareth 20 (5-9.9%) an emulsifying agent, and surfactant.

Ascorbyl palmitate is an anti oxidant.

CLAIMS

1. Use of shark liver oil comprising alkyl glycerols for the preparation of a drug for local treatment of skin diseases selected from summer sore, sarcoids, greasy heels, rain scalds, saddle sore and girth galls in domestic animals.
2. The use according to claim 1, of from 1 to 100 % of crude or refined shark liver oil.
3. The use according to claim 1 and 2 of crude or refined shark liver oil comprising of up to 100% of alkyl glycerols.
4. The use according to any of claims 1 to 3 for the preparation of a drug for the treatment of summer sore in the skin of horses.
5. The use according to any of claims 1 to 3 for the preparation of a drug for the treatment of Equine sarcoids.
6. A method of treatment of domestic animals suffering from skin diseases selected from summer sore, sarcoids, greasy heels, rain scalds, saddle sore and girth galls by application of a preparation comprising from 1 to 100 % of crude or refined shark liver oil including alkyl glycerols.
7. The method according to claim 6 of treatment of domestic animals suffering from skin diseases selected from summer sore, sarcoids, greasy heels, rain scalds, saddle sore and girth galls by local application of a preparation comprising up to 100 % of alkyl glycerols.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/SE 99/00820

A. CLASSIFICATION OF SUBJECT MATTER

IPC6: A61K 35/60, A61K 9/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC6: A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE,DK,FI,NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0321428 A2 (HÄLSOPRODUKTER LARS KÄRNERUD AB), 21 June 1989 (21.06.89) --	1-7
A	US 4447418 A (LILLA A. MADDUX), 8 May 1984 (08.05.84) --	1-7
A	US 5554361 A (GARY W. DIXON), 10 Sept 1996 (10.09.96), column 20, line 60 - line 65; column 26 - column 27, example 3 -----	1-7

☐ Further documents are listed in the continuation of Box C.☒ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

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Date of the actual completion of the international search

24 August 1999

Date of mailing of the international search report

01 -09- 1999

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE99/00820

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 6-7
because they relate to subject matter not required to be searched by this Authority, namely:

see next page
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE99/00820

Claims 6-7 relate to methods of treatment of the human or animal body by therapy (Rule 39.1(iv)).
Nevertheless, a search has been executed for these claims. The search has been based on the alleged effects of the compounds.

INTERNATIONAL SEARCH REPORT
Information on patent family members

02/08/99

International application No.

PCT/SE 99/00820

Patent document cited in search report			Publication date	Patent family member(s)		Publication date
EP	0321428	A2	21/06/89	CA	1316460 A	20/04/93
				SE	8705035 A	18/06/89

US	4447418	A	08/05/84	NONE		

US	5554361	A	10/09/96	US	5700457 A	23/12/97
